PATENT COOPERATION TREATY 2026-4303 PC

Lombillo

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	23.10.2001
Applicant's or agent's file reference 2026-4303PC	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/15527	02/06/2000	04/06/1999

Applicant
NATIONAL INSITUTES OF HEALTH

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hingel, W Tel.+49 89 2399-8717

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
2026-4303PC		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/15527	02/06/2000	04/06/1999
International Patent Classification (IPC) or national classification and IPC C12N15/86		
Applicant NATIONAL INSITUTES OF HEALTH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02/01/2001	23.10.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Paresce, D Telephone No. +49 89 2399 8995

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/15527

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-37 as originally filed

Claims, No.:

1-21 as originally filed

Drawings, sheets:

1/19-19/19 as originally filed

Sequence listing part of the description, pages:

1-36, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

   Novelty (N) Yes: Claims 1-10, 14-21

	No:	Claims	11-13
Inventive step (IS)	Yes:	Claims	1-10, 14-21
	No:	Claims	11-13
Industrial applicability (IA)	Yes:	Claims	1-21
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Lack of unity (Rule 13.1 PCT):

The documents mentioned in this communication are numbered as in the search report, i.e. D1 corresponds to the first document of the search report.

The IPEA agrees with the objection put forward by the Search Division as to lack of unity (Rule 13.1 PCT). The IPEA is also of the opinion that the present set of claims relates to two different inventions (see International Search Report). The separate inventions/groups of invention are:

1) Claims 1-6, 11-13 (completely) and 9-10, 14-21 (partially) are directed to a nucleic acid molecule comprising a chimeric virus genome, said genome being a BVDV genome in which the structural region of the BVDV genome has been replaced by the structural region of a hepatitis C virus genome. The claims are further directed to a DNA construct comprising said molecule, an RNA transcript of said DNA construct, a host cell transfected with said DNA construct or RNA construct, a chimeric HCV-BVDV produced by said host cell and a composition comprising said virus.

2) Claims 7-8 (completely) and 9-10, 14-21 (partially) are directed to a nucleic acid molecule comprising a chimeric virus genome, said genome being a BVDV genome in which the non-structural region of the BVDV genome has been replaced by the non-structural region of a hepatitis C virus genome. The claims are further directed to a DNA construct comprising said molecule, an RNA transcript of said DNA construct, a host cell transfected with said DNA construct or RNA construct, a chimeric HCV-BVDV produced by said host cell and a composition comprising said virus.

The general inventive concept underlying the two above identified inventions of the present application can be seen as the provision of chimeric BVDV-hepatitis C virus genomes. This general inventive concept, however, is not considered novel because, as illustrated by D1, the concept of providing chimeric BVDV-hepatitis C virus genomes was known in the prior art. In D1, a functional clone of BVDV was used to construct and characterize a series of 5' NTR chimeras with sequences derived from the hepatitis C virus (HCV) as well as other flaviviruses. The results

of this study help to define the requirements of a functional BVDV 5' NTR and provide replication-competent BVDV-HCV chimeras dependent on a functional HCV internal ribosome entry site (see D1, p. 1419).

In view of D1, the problem underlying the present application is considered as the provision of further BVDV-HCV chimeric genomes. One solution to this problem provides a chimeric virus genome, said genome being a BVDV genome in which the structural region of the BVDV genome has been replaced by the structural region of a hepatitis C virus genome. The second solution is considered the provision of a chimeric virus genome, said genome being a BVDV genome in which the non-structural region of the BVDV genome has been replaced by the non-structural region of a hepatitis C virus genome.

In response to an invitation to pay additional fees (see Form PCT/IPEA/405), the Applicant paid the additional examination fees. Consequently the international preliminary examination will be based on claims 1-21 of the present application.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) Novelty: Article 33(2) PCT

D1 discloses the construction and characterization of a series of BVDV-hepatitis C virus (HCV) 5' NTR chimeras. The results of this study help to define the requirements of a functional BVDV 5' NTR and provide replication-competent BVDV-HCV chimeras dependent on a functional HCV internal ribosome entry site (see D1, p. 1419).

D2 discloses chimeric genomes of poliovirus in which the cognate internal ribosomal entry site element was replaced by genetic elements of hepatitis C virus (see abstract).

D3 presents a review of flavivirus research and, in particular, flavivirus vaccines. D3 mentions the development of chimaeric viruses as potential vaccine

candidates. D3 discloses dengue virus chimeras, TBE/dengue virus chimeras, poliovirus expression vectors and mentions developments in generating RNA viruses from cloned cDNA (see p. 975).

D4 and D5 describe the sequence and structural elements of BVDV (see abstracts).

The subject-matter of claims 11-13 is not considered new in the sense of Article 33(2) PCT for the following reasons: The subject-matter of these claims, when interpreted in the broadest sense possible, covers any polypeptide encoded by a BVDV nucleic acid sequence or a hepatitis C virus nucleic acid sequence. BVDV and hepatitis C virus proteins were known in the prior art at the priority date of the present application (see D1-D5). Therefore, these claims are not considered novel.

D1 discloses BVDV-hepatitis C virus (HCV) chimeras in which the nontranslated regions of the BVDV genome were replaced with those from HCV. D1 does not disclose BVDV-hepatitis C virus (HCV) chimeras in which the structural or non-structural region of the BVDV genome is replaced with the structural or non-structural region of the HCV genome. The subject-matter of claims 1-10, 14-21 has not, in fact, been made available to the public by any of the available prior art documents and can therefore be regarded as novel.

The subject-matter of claims 1-10, 14-21 cannot be derived from the available prior art in an obvious manner and therefore complies with the requirements of Article 33(3) PCT.

VI: Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO9955366	04.11.99	23.04.99	24.04.98